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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,673	01/16/2004	Danila Valmori	LUD 5483.7 DIV (10316191)	7395
24972 7590 04/14/2009 FULBRIGHT & JAWORSKI, LLP 666 FIFTH AVE NEW YORK, NY 10103-3198			EXAMINER DIBRINO, MARIANNE NMN	
			ART UNIT 1644	PAPER NUMBER
			MAIL DATE 04/14/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/758,673	Applicant(s) VALMORI ET AL.	
	Examiner DiBrino Marianne	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/28/09 & 11/18/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19, 21 and 25-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19, 21, 25, 26, 29 and 30 is/are rejected.
- 7) ☒ Claim(s) 27, 28 and 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/28/09 has been entered.

Applicant's response filed 11/18/08 is acknowledged and has been entered.

2. Claims 19, 21 and 25-31 are presently being examined.

3. Applicant's amendment filed 11/18/08 has overcome the prior rejection of record of claims 19, 21 and 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (*i.e.*, the new matter rejection).

4. Applicant's amendment filed 11/18/08 has overcome the prior rejection of record of claims 19, 21, 25 and 26 under 35 U.S.C. 112, first paragraph, scope of enablement.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 19, 21, 25, 26, 29 and 30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,368,857 B1 in view of Gilbert *et al* (Nature Biotech. 1997, 15: 1280-1284, of record) and US Patent No. 5,662,907 (of record).

The instant claims are drawn to a method for inducing proliferation of CTL, said method comprising contacting a sample containing CTLp taken from a patient with a tumor which is a melanoma with a polytope comprising the amino acid sequence of one of SEQ ID NO: 7-11 or 16, wherein said amino acid sequence forms a complex with an HLA molecule, including HLA-A*0201, and a sample of cells which present HLA molecules on their surfaces and which process said polytope to Melan-A peptides which complex with said HLA molecules, wherein the complexes of said HLA molecules and the amino acid sequence of one of SEQ ID NO: 7-11 or 16 induce proliferation of CTL.

Claims 1-5 of U.S. Patent No. 6,368,857 B1 do not recite that the method comprises contacting a sample comprising CTLp with a polytope, and a sample of cells which present HLA molecules on their surfaces and which process said polytope to Melan-A peptides that complex with said HLA molecules, including wherein the HLA molecule is HLA-A2 recited in instant claim 21 (*i.e.*, HLA-A*0201).

Gilbert *et al* teach constructing polytope proteins comprising one or more class I MHC-restricted CTL epitopes and the p1 protein of the retrotransposon Ty1 of *S. cerevisiae*, and optionally also comprising CD4 epitopes. Gilbert *et al* teach that their polytope protein consists of a single protein species that can be simply produced in yeast at high yields and carries a string of up to 15 defined CTL epitopes from *Plasmodium* species, said polytope protein effectively primes protective CTL responses in mice following a single administration without adjuvant. Gilbert *et al* teach that effective processing of epitopes from the string was demonstrated *in vitro* and *in vivo* and was not affected by flanking sequences. Gilbert *et al* teach that using minimal epitopes to produce vaccines instead of whole antigens enables the immune response to be directed towards conserved regions of antigens. Gilbert *et al* teach that in mice, the response towards the polyepitope protein is long lasting and can be boosted, that in humans they are safe and elicit cellular and proliferative responses to the vaccine. Gilbert *et al* teach that in humans, use of alum adjuvant impairs CTL response, but in a phase I trial where no adjuvant was used, CTL responses were induced to the polyepitope protein (see entire article, especially abstract, introduction, discussion).

US Patent No. 5,662,907 discloses contacting CTL with an immunogenic peptide *in vitro* and then reintroducing the activated cells into a patient with cancer, such as melanoma, or that alternatively, the peptides can be used as a vaccine to induce an immune response *in vivo*, or a combination of both methods may be used. US Patent No. 5,662,907 discloses that the peptides may be used therapeutically to elicit CTL responses to melanoma in the form of a peptidic vaccine, or for *ex vivo* therapy in which CTL are induced in tissue culture and used for adoptive immunotherapy. US Patent No.

5,662,907 discloses that *ex vivo* CTL responses to a tumor antigen are induced by incubating in tissue culture the patient's CTL precursor cells together with a source of antigen presenting cells (APC) and the appropriate immunogenic peptide. US Patent No. 5,662,907 discloses using more than one peptide in a vaccine or using heteropolymers of different peptides for stimulating CTL responses for the advantage of increased immunological reaction and the additional ability to induce CTL that react with different antigenic determinant of the tumor cells, and different types of APC, including autologous PBMC, pAPC such as dendritic cells and activated B cells (especially column 2 at lines 26-33, column 4 at lines 8-16, column 12 at lines 13-44, column 13 at lines 19-37).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made and used a polytope such as taught by Gilbert *et al* and disclosed by US Patent No. 5,662,907 in the method of claims 1-5 of U.S. Patent No. 6,368,857 B1, *i.e.*, to have made a complex of the peptide and HLA-A2 using a polytope peptide that would be processed to form the said complex.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate CTLp *ex vivo* as disclosed by US Patent No. 5,662,907 using a polypeptide peptide with multiple CTL epitopes taught by both references to be advantageous in increased immune response with multiple CTL specificities to tumor antigens, and for generating CTL *ex vivo* for adoptive immunotherapy or the combination therapy disclosed by US Patent No. 5,662,907.

7. Claims 27, 28 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
April 6, 2009

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644